REMARKS

Applicant respectfully requests reconsideration.

Claims 1-41 were previously pending in this application with claims 2-5, 7-9 and 15-41 being withdrawn from further consideration.

Claim 10 is now cancelled without prejudice or disclaimer.

Claims 1 and 11-14 are now amended. Support for the amendment to claim 1 can be found in originally filed claim 10. Claims 11-14 are amended in part to depend from a pending claim and/or to have proper antecedent basis to the claim from which each depends.

Claim 42 is added. Support for this claim can be found at least in Figs. 1(x), 1(xi), I(xvix), 1(xx), and 8.

No new matter has been added.

Claims 1, 6, 11-14 and 42 are currently being examined.

Rejection under 35 U.S.C. §112, second paragraph

Claims 10-14 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite. Claim 10 is now cancelled. Claim 1 is now amended to incorporate limitations from claim 10. As now amended, claim 1 recites a tapered channel and a plurality of side channels. Claims 11-14 are amended to depend from a pending claim and to refer to the tapered channel. The claims are definite.

Reconsideration and withdrawal of this rejection is respectfully requested.

Rejection under 35 U.S.C. §102

Claims 1 and 6 are rejected under 35 U.S.C. §102 as being anticipated by Lyon et al. (Anal. Chem. Vol. 69, 16:3400-5).

Claim 1 is amended herewith to include limitations of claim 10. This amendment is made in the interest of expediting prosecution and without conceding the Examiner's characterization of Lyon et al. Applicant reserves the right to pursue the subject matter of the originally filed claims in one or more continuing applications.

Lyon et al. does not teach, inter alia, the limitations of claim 1, as now amended. The Examiner has acknowledged this by not rejecting previously pending claim 10 in view of Lyon et al. Accordingly, Lyon et al. does not anticipate claim 1, as now amended, nor claim 6 which depends from claim 1.

Reconsideration and withdrawal of this rejection is respectfully requested.

Rejection under 35 U.S.C. §103

Claims 1, 6 and 10-14 are rejected under 35 U.S.C. §103(a) as being unpatentable over Oefner et al. (U.S. Patent No. 5,846,832).

Oefner et al. teaches an apparatus and method for shearing nucleic acids and thereby producing a subset of nucleic acids having a defined size distribution. Oefner et al. describes its apparatus as containing "a capillary with an orifice near the outlet end of the capillary". Examples of the apparatus, including the capillary and orifice, are shown in Figs. 2A, 2B, 2C and 2D. In each instance, the transition from the capillary to the orifice is abrupt with a stepped rather than gradual diameter change. In none of these examples is the capillary tapered. Oefner et al. teaches that the abrupt change between the capillary and orifice diameter is required in order to generate size-fractionated nucleic acids. For example, in column 2, lines 55-65, Oefner et al. teaches that

> "In one embodiment, the orifice is the channel of a second capillary attached at the outlet end of the first capillary. Since the second capillary is functioning as the orifice, it has an inner diameter that is at least about a factor of two smaller that the inner diameter of the first capillary; preferably, the diameter of the second capillary is at least about 3 times smaller than that of the first capillary. For efficient generation of fragments below about 4,000 base pairs, the diameter of the second capillary is preferably at least about 5 times smaller than the diameter of the first capillary."

Thus, Oefner et al. teaches that the inner diameter differences between the capillary and the orifice contribute to the degree of size-fractionation that can be achieved.

The Examiner concedes that Oefner et al. does not teach a tapered channel. However, the Examiner considers that it would have been obvious to taper the capillary of Oefner et al. because this was an alternative embodiment proposed by Oefner et al. The Examiner's position relies on the statement by Oefner et al. in column 2 lines 65-67 that

> "The transition in I.D.s (internal diameters) from the first capillary to the orifice is preferably abrupt, rather than gradually tapering to a smaller diameter."

Applicant respectfully disagrees. Applicant notes that the rejection is one of obviousness and not novelty. Thus, clearly and correctly, the Examiner acknowledges that Oefner et al. does not teach a tapered channel. The cited passage therefore does not provide an alternative embodiment, as suggested by the Examiner.

More importantly, Oefner et al. does not provide any rationale for using a tapered channel. Quite to the contrary, Oefner et al. clearly teaches that abrupt changes in internal diameter are preferred *in contrast* to gradual tapering. This is only reinforced by the embodiments and examples in Oefner et al., all of which involve an abrupt diameter change from capillary to orifice as well as constant inner diameters of capillaries and orifices (if such orifices have a discernable length).

Moreover, Oefner et al. repeatedly and consistently distinguishes the orifice from the capillary. This distinction argues against a gradual tapering between these two elements. For example, in addition to the cited passage above, Oefner et al. states that

> " "orifice" is used in the present application to refer to a constriction in a tube or capillary effective to reduce the inner diameter of the tube or capillary by at least a factor of about 2; preferably al (sic) least about 4. Examples of an orifice include a hole in a disk positioned in a capillary, as well as a capillary with a small internal diameter connected to a capillary with a larger internal diameter." (Column 7 lines 17-24.)
>
> "... other factors being equal, the smaller the size of the orifice, the smaller the mean size of the sheared fragments." (Column 5 lines 30-32.)
>
> "The flow rate and orifice diameter are determined ... to generate a desired size distribution ..." (Column 5 lines 41-44.)
>
> "The second capillary has an inner diameter **168** that is considerably smaller that (sic) the inner diameter of the first capillary, and accordingly, constitutes an orifice." (Column 9 lines 5-7.)
>
> "The mean size of the distributions obtained depends primarily on the diameter or size of the orifice ... " (Column 10 lines 11-12.)
>
> "The net shear force experienced by the polynucleotide chain is determined primarily by the diameter of the orifice, by the flow rate into and through the orifice, and, to a lesser extent,

by the length of the orifice in capillary orifices. The smaller the orifice, the greater the shear ... " (Column 10 lines 26-30.)

" ... it is possible, according to the teachings herein, to generate size distributions with mean fragment sizes defined by the static parameters of the shearing apparatus (i.e., orifice diameter, ... " (Column 11 lines 27-30.)

When read as a whole, including in particular the cited passages above, one of ordinary skill in the art recognizes that the apparatus of Oefner et al. requires a capillary that is distinct from, and has a greater inner diameter than, an orifice. There would be no rationale for using a gradual tapering in the apparatus of Oefner et al. for a number of reasons.

First, a gradual tapering between the capillary and the orifice would render the capillary and the orifice indistinct. This is clearly not what Oefner et al. has intended.

Second, one of ordinary skill in the art would not understand how to apply the teachings in Oefner et al. to such tapered inner diameters, particularly since Oefner et al. repeatedly emphasizes the need for abrupt diameter changes. For example, would one of ordinary skill in the art understand, in the context of a gradual tapering, where the capillary ended and where the orifice began, and where to measure the capillary and orifice diameter?

Third, if the capillary was tapered and continuous with the orifice, or if the transition from the capillary to the orifice was tapered, the shearing apparatus of Oefner et al. would not operate as intended (i.e., it would not generate sheared polynucleotides of a particular size range) because it is the sharp difference between the inner diameters of the capillary and the orifice that contributes to the shearing function. The apparatus of Oefner et al. induces shear breakage of polynucleotides. Modifications to the apparatus that interfere with this intended function would not be obvious.

For at least these reasons, it would not have been obvious to make the capillary of Oefner et al. tapered, and as a result Oefner et al. does not render obvious the rejected claims. Oefner et al. also does not render obvious new claim 42 for at least these same reasons and because Oefner et al. does not provide the limitations of this claim.

Reconsideration and withdrawal of this rejection is respectfully requested.

Double Patenting Rejection

Claim 1 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-13 of U.S. Patent No. 6,696,022. As noted above, Applicant has amended claim 1 to include limitations of claim 10, namely side channels. The Examiner had previously concluded that the species of instant claims 2-9 were patentably distinct from the species of instant claims 10-14. Claims 1-13 of the '022 patent recite a limitation from instant claim 3. Accordingly, claim 1 as now amended is patentably distinct from the cited claims, and the rejection on the basis of nonstatutory obviousness-type double patenting is improper. 35 U.S.C. 121. Consistent with this, claim 10 was not rejected by the Examiner on double patenting grounds.

Reconsideration and withdrawal of this rejection is respectfully requested.

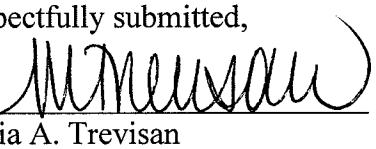
CONCLUSION

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, the Director is hereby authorized to charge any deficiency or credit any overpayment in the fees filed, asserted to be filed or which should have been filed herewith to our Deposit Account No. 23/2825, under Docket No. C0989.70030US01.

Dated: September 4, 2009

Respectfully submitted,

By 

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